

LOCARNINI et al
Serial No. 09/306,420

25. (new) A variant according to claim 23 wherein the amino acid mutation is in the B domain and/or the C domain of the HBV DNA polymerase.

26. (new) A variant according to claim 23 comprising a mutation in one or more of amino acids within the sequence:

Q/K T Y/F G R/W KLHL Y/L S/A HPI I/V LGFRK I/L PMG V/G GLS PFLL

AQFTSAI C/L S (SEQ ID NO:25)

of HBV DNA polymerase.

27. (new) A variant according to claim 26 comprising a mutation in one or more amino acids within the sequence:

S/A HPI I/V LGFRK I/L PMG V/G GLSPFLLAQFTSAIC/L S (SEQ ID NO:44)

of HBV DNA polymerase.

28. (new) A variant according to claim 23 comprising a nucleotide sequence which encodes a DNA polymerase having the amino acid sequence:

X₁HPIX₂LGX₃RKX₄PMGX₅GLSX₆FLX₇AQFTSAX₈X₉ (SEQ ID NO:27)

X₁₀FX₁₁YX₁₂DDX₁₃VLGAX₁₄X₁₅ (SEQ ID NO:28)

wherein X₁ is S or A;

X₂ is I or V;

X₃ is F or L;

X₄ is I or L;

LOCARNINI et al
Serial No. 09/306,420

X₅ is L or V or G;

X₆ is P or L;

X₇ is L or M;

X₈ is I or L;

X₉ is C or L;

X₁₀ is A or V;

X₁₁ is S or A;

X₁₂ is M or I or V;

X₁₃ is V or L or M;

X₁₄ is K or R; and/or

X₁₅ S or T;

and wherein said variant exhibits reduced sensitivity to a nucleoside analogue, such as famciclovir (penciclovir) and/or lamivudine (3TC).

29. (new) A variant according to claim 23 having a mutation in one or more of amino acids 118 to 169 or 169 to 207 of HBV surface antigen.

30. (new) A variant according to claim 29 comprising a DNA polymerase having the amino acid sequence:

X₁₆TX₁₇X₁₈X₁₉KLHLX₂₀X₂₁HPIX₂₂LGX₃RKX₄PMGX₅GLSX₆FLX₇AQFTSAX₈X₉.....

(SEQ ID NO:42)

X₁₀FX₁₁YM₁₂DDX₁₃VLGAX₁₄X₁₅ (SEQ ID NO:43)

LOCARNINI et al
Serial No. 09/306,420

wherein:

- X₁₆ is Q or K;
- X₁₇ is Y or F;
- X₁₈ is G;
- X₁₉ is R or W or E;
- X₂₀ is Y or L;
- X₂₁ is S or A;
- X₂₂ is I or V;
- X₃ is F or L;
- X₄ is I or L;
- X₅ is L or V or G;
- X₆ is P or L;
- X₇ is L or M;
- X₈ is I or L;
- X₉ is C or L;
- X₁₀ is A or V;
- X₁₁ is S or A;
- X₁₂ is M or I or V;
- X₁₃ is V or L or M;
- X₁₄ is K or R; and/or
- X₁₅ S or T;

and wherein said variant exhibits reduced sensitivity to a nucleoside analogue, such as famciclovir (penciclovir) and/or lamivudine (3TC).